THE TREATMENT OF WOUND INFECTIONS.*

BY

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ATTENTION is being drawn at the present time to the study of the physiological aspect of the treatment of wound infections, and, as a result, new methods, to replace old, have been suggested. In particular, Sir Almroth Wright advocates very strongly giving up treatment by antiseptics for treatment by salt solutions. He does this chiefly on the ground of laboratory experiments, laying it down in respect to treatment that "where the results are neither brilliantly successful nor the reverse . . . we shall be well advised if we guide ourselves, when this is unambiguous, by the verdict of laboratory experiments." Although I have been working with him, I am unable to agree that his experiments conform to this standard, and would for that reason put forward points which appear worthy of further consideration. These relate to: (1) Measures which affect the flow of lymph; (2) measures which affect the flow of pus; (3) antiseptics.

1. *Measures which Affect the Flow of Lymph.*

In his first lecture on the treatment of wounds Sir Almroth Wright maintained "that we have at disposition an agency for powerfully increasing the outflow of lymph," and asserted that a 5 per cent. solution of common salt "brings into play osmotic forces, and 'draws' the lymph out of the walls of a wound by a *vis a fronte*." In his second lecture, as a result of the criticism that osmotic forces would determine the flow of water and not of lymph, he appeared to give up the notion of osmosis, but otherwise maintained his position. At this lecture he showed four experiments to "bring clearly before the eye the drawing power of salt." For the first, he took a capillary tube open at both ends with an additional opening at its middle. This tube he filled with strong salt solution, and, holding it horizontally, dipped it for a few seconds into a watery solution of methylene blue. On taking the tube out he found that more methylene blue had passed in through the three openings than had happened in the case of a control tube which contained water instead of salt solution. This result we should expect, since salt solution is heavier than water. The salt solution would, for this reason, tend to fall out of the tube, and consequently the methylene blue solution would run in to take its place. The same explanation holds in the case of the second experiment, which was as follows: A piece of glass tubing, plugged with moist cotton-wool, was placed vertically in a vessel containing a watery solution of methylene blue. It was found that the methylene blue travelled up the tube, but travelled higher when salt was placed on the top of the plug. In the third experiment Sir Almroth Wright took a "stab" of watery agar, and on the top placed a cube of salt. In some twelve hours an interchange had taken place, salt passing into the agar and water to the salt. This he gave as a demonstration of what he expected—namely, "a process of barter in which salt and water should be exchanged, not in volumetric equivalents, but in the ratio of very many volumes of fluid for one of the solid." As a matter of fact, the volume of fluid in such a case is not greater than the volume of solid, and the experiment is merely a demonstration of the diffusibility of salt in agar. The fourth experiment was similar, but in this case the stab consisted of blood agar. Here the presence of the albuminous substances in the fluid which collected above the agar showed only that such substances diffuse in agar in the same way as salt, and not that salt draws lymph. It is therefore clear that these experiments do not support the view that hypertonic solution will draw lymph out of a wound.

Again, Sir Almroth Wright, in his discourse, asserted that it was "confusion of thought" which led to the belief "that it is the interposition of the sieve which confers upon salt the power of drawing water to itself." Such an assertion is really a denial of Newton's third law, which lays it down that action and reaction are equal and opposite. For it follows from this law that salt would be drawn to water by forces equal to any which would draw water to salt. Consequently, unless a sieve supported and held back salt, while not at the same time preventing the passage of water, there could not be such a process of barter as Sir Almroth Wright suggests. It is plain, then, that the only sense in which salt can be said to draw "water" to itself is that recognized when such a process as osmosis takes place. But salt cannot be said to draw lymph to itself even by osmosis, because albuminous substances cannot pass through membranes impermeable to salt. On the contrary, it might be said that since animal membranes are usually permeable to crystalloids and not to colloids an albuminous substance may by osmosis "draw" salt to itself.

Having seen that salt does not draw lymph by a *vis a fronte*, we may examine how the outflow can be influenced. We shall only deal with those ways which are clearly physical. For these to be operative, we must presume that the lymph spaces and channels, potential and otherwise, are open to the surface, and that a fluid pressure greater than atmospheric tends to drive lymph out through them. The flow will then be at a rate depending on the pressure in the tissues and on the number and size of the channels. As regards the pressure, it is plain that this will vary with the hyperaemia, and so we may expect that any measure which favours hyperaemia will also act as a lymphagogue. Again, as regards the channels, we see that they may be obstructed (1) by dried lymph on the surface blocking the outlets; (2) by the cellular walls coming together and obliterating such channels. The application of any moist dressing will usually remedy the first, and is as a rule sufficient. In this connexion it must not be thought that moist coagulated lymph will necessarily prevent drainage. After all, it is merely a meshwork of fibrin in which the leucocytes can move and function. It is hardly comparable with a membrane, and is pervious unless it becomes blocked by pus cells. The obstruction due to this and to the obliteration of the channels can be relieved if we can abstract fluid from the cells. This can be done by the application of hypertonic solutions, which would cause an osmotic diffusion of water out of the cells. The cells would then shrink and the obliterated channels open up, just as the ground is fissured in dry weather. The result would be that the lymph would have free passage to the surface and the lymph-bound condition be relieved. This action of hypertonic solutions can readily be demonstrated by trying to filter fluids through agar containing blood corpuscles. Owing to the osmotic crenation and shrinkage of the corpuscles which they cause, hypertonic solutions go through comparatively readily, while the isotonic are held back.

But it is hardly to be expected that the direct osmotic effect of salt in a wound will be more than a very superficial one, for, once a flow is established, the current of lymph outwards will tend to counteract the diffusion of salt inwards. Thus, as soon as the surface becomes pervious, the presence of hypertonic solutions cannot be expected still further to increase the flow. Again, it does not necessarily happen that the osmotic effect of hypertonic solutions will always produce conditions favourable to a flow. From a clinical point of view, this is made clear by Colonel H. M. W. Gray,[1] who, at Rouen, in a lecture strongly advocating the use of hypertonic salt solution as a lymphagogue, gave away much of his case by pointing out that salt tabloid packs, so far from producing a flow, frequently became dry after twenty-four hours.

It may be observed here that the effect of hypotonic fluids, such as tap water, hydrogen peroxide, and iodine solutions, have the opposite effect to hypertonic fluids, and would cause the surface cells to swell. This swelling may be expected to bring about a diminished flow of lymph. It is therefore desirable that the excipient used for antiseptics should be isotonic with the blood fluids. For this reason we ought to dilute antiseptics with physiological saline, unless they are incompatible, and not, as is usually done, with water.

2. *Measures which Affect the Flow of Pus.*

Here, again, Sir Almroth Wright claims that he has a specific, this time in physiological saline, asserting that "the white corpuscles are carried forward by a chemiotactic movement in the direction of the free surface upon

* Read at the Royal Society of Medicine, Pathological Section, on May 2nd, 1916 (see p. 689).

which the physiological solution has been imposed." I would venture, however, to examine in fuller detail the experiments on which he bases this claim, and whether it is warranted by them.

Taking flat capillary tubes containing unclotted blood, he centrifugalized this before it had time to clot. When clotting had taken place there was then in the tube a clot consisting of a red corpuscular portion (*a*), a white plasma portion (*c*), and between these, joining them, a narrow portion containing white corpuscles (*b*). He then superimposed upon these clots a "chemiotactic agent," such as saline, and incubated them. The clots were afterwards removed from the tubes, mounted on slides, and stained. It was observed in many cases that, if the temperature was in the neighbourhood of body temperature, the leucocytes had wandered or emigrated into the white clot. It was on experiments of this nature that Sir Almroth Wright based his statements regarding chemiotaxis.

We may get help in understanding the behaviour of the leucocytes in these experiments if we consider the ways in which the clot tends to contract, and, for this purpose, it is what happens in the neighbourhood of the leucocytic layer of the clot which is of importance as once the leucocytes have moved well out into the white clot they appear to remain there. Sometimes, as Sir Watson Cheyne points out,[2] there is no contraction (Fig. 1, A). At other times contraction takes place at the junction of the red and white clots (Fig. 1, B, C), and a neck containing most of the leucocytes is formed. This neck may lie wholly free in serum (Fig. 1, B), or partially in contact with the walls of the tube (Fig. 1, C). When it lies wholly free in serum, it becomes highly probable that the wandering movements of the leucocytes will result in their finding a way laterally out of the clot into the serum more readily than along the axis, and thus we would expect to find, in such a case, no emigration. On the other hand, when the neck of the clot lies partly in contact with the tube, the leucocytes in that situation would not be able to pass out of the clot, and so they would be more likely to travel along the axis and show emigration. These expectations accord with what is actually seen to take place. In my own experiments I found in some cases practically no polynuclear cells in the white clot, and only a few mononuclear near the neck. This occurred both with and without the addition of the chemiotactic agent. In other cases the leucocytes travelled along the clot, especially the more active polynuclear. This also occurred both with and without the addition of the chemiotactic agent. Some of the specimens, showing ultimately no emigration, where no chemiotactic agent had been applied, I examined from time to time on a warm stage, where the movements of the leucocytes could be watched. At first near the neck, they could be seen moving actively in all directions, but later they disappeared out of the clot. When mounting these specimens, I collected the serum which had exuded from the clot, and found a very large number of leucocytes in the exudate. Subsequent examination of the tubes, which, after the clot had been removed, were immediately filled with fresh serum, also revealed large numbers of leucocytes adhering to the walls and showing active movements. Hence the polynuclear leucocytes do, without the application of a chemiotactic agent, wander into the clot and then out into the serum. It is clear, therefore, that Sir Almroth Wright can hardly be justified in supposing that emigration due to wandering or "eleutherotropic" movement is predominantly mononuclear and that polynuclear emigration is chemiotactic. This variable loss of leucocytes from the clot to the serum, clearly independent of any possible chemiotactic influence, shows that it is as futile to aim at measuring quantitatively the emigration movements and chemiotactic effects by estimating the number of leucocytes which remain in the white clot at different distances from the red as it would be to estimate the total number of a company after an unknown proportion had retired. But even when free emigration takes place in the presence of physiological saline it cannot be said to be due to chemiotaxis, for the distance traversed by the leucocytes is little or no greater than when no fluid but serum is present, whereas if such emigration were due to chemiotaxis—that is, "a directed movement along a particular axis undertaken under the direction of a chemical stimulus"—one would expect great differences. The small differences that are occasionally seen may be explained by a slight effect which physiological saline may possibly have in increasing the non-directed wandering movements of the leucocytes. This effect is apparently shown in some specimens obtained by mixing saline with blood before it clots, circumstances in which there could be no chemiotaxis. But even admitting this stimulation, it is doubtful whether it is of any value. For the leucocytes would not start their wanderings in larger numbers, but only travel faster through the infected tissues, and act there for a shorter time. Again, physiological saline would not increase the all-important function of phagocytosis. I submit, therefore, that laboratory results, as yet, give no grounds for asserting that we have in physiological saline an agent which will advantageously affect the activities of the leucocytes and the flow of pus into a wound.

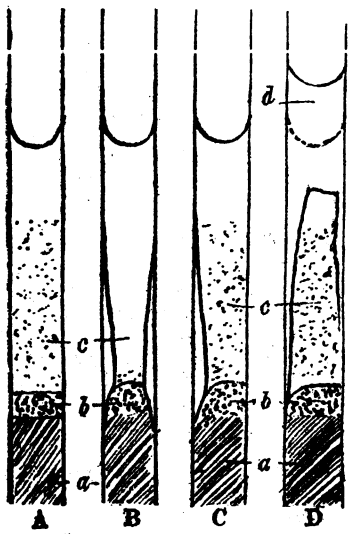

FIG. 1.—Emigration tubes showing different types of contraction. (*a*) Red clot, (*b*) leucocytic layer, (*c*) white clot, (*d*) superimposed fluid. A, No contraction; free emigration shown. B, Contraction with the formation of a neck at the leucocytic portion of the clot, which lies free in serum; emigration is not shown in this. C, Contraction similar to B, but the neck is partly in contact with the tube; emigration shown. D, Chemiotactic agent superimposed; retraction of clot along its axis; leucocytic layer in contact with the tube; emigration shown; this clot is not so likely to contract in mounting, so that the distance which leucocytes traverse would appear greater than in those from A and C.

On the other hand, there is no difficulty in agreeing that strong antiseptics, bacterial suspensions, and, above all, hypertonic solutions do act in suppressing leucocytic movements. This is clearly shown by experiments made by mixing the blood and the test fluid in the emigration tubes before clotting takes place. Such experiments show that some antiseptics—such as carbolic acid—powerfully suppress emigration, whilst others—such as mercuric salts and the neutral hypochlorous solutions—have comparatively little action. But of more practical significance in determining the possible injurious effects produced by the various applications on the physiological processes is the observation made on the wound itself as to whether there is a good flow of laudable pus. If there is, we may be sure that the application is not doing much harm to the tissues, and that the physiological processes remain active. In this connexion it may be noted that Sir Almroth Wright points out "that the practitioner of to-day has been educated up to expect to find, within a few hours after washing out an infected wound with antiseptics, as much pus as when he last came to dress it"; and that hypertonic salt solution will, as long as its concentration is maintained, arrest all suppurative processes and "give us a wound as clean and as free from pus as meat." The inevitable conclusion from this is that in practice, treatment by hypertonic saline, by interfering with the activities of the leucocytes, renders ineffective the only defence there is against the streptococcus and staphylococcus, whilst, with the application of an antiseptic or of physiological saline, this defence comes again into action.

But some do not view with satisfaction a good flow of pus from a badly infected wound, and it is not uncommon to hear the contemptuous expression "pus poultice." Certainly if the pus is stale, and has become "corrupted," it is noxious, but if fresh, it is efficiently doing its work of combating the organisms. Our aim must therefore be to remove the pus before it becomes corrupted, and if possible to destroy the organisms which corrupt it. The methods of removing pus are, of course, by constant irrigation and occasional flushing, and in deciding between these, it must be remembered that the use of irrigating fluids, even of physiological saline, if delivered below body temperature, will do harm by retarding the activities of the leucocytes. The possibility of destroying the organisms brings us to the consideration of antiseptics.

3. *Antiseptics.*

The attempt to destroy organisms in wounds is made in two ways—(1) by washing out with lotions, (2) by the application of dressings. In connexion with the washing out of a wound, it will be recognized that, although, as has been observed, the greater part of the wash will be thrown down the sink, a residue will remain in the recesses and pockets; and also that even on the most exposed surfaces some lotion will remain, wetting the films of pus adhering to those surfaces. These will continue to be a source of infection unless they can be sterilized. We have thus to consider the effect of antiseptics on them. In the case of the residue, there is a comparatively large quantity of antiseptic mixed with a small amount of pus, and for the purpose of estimating the effect of the antiseptics, I took it that the conditions of the following experiment were analogous.

Mixtures of one part of pus and nine of antiseptic were made, and, after ten minutes, 10 c.mm. planted in tubes of liquid agar at 42° C. After they were thoroughly shaken, the tubes were sloped and the agar allowed to set. They were then incubated at 37° C., and after a period were examined for colonies. It was found that when the antiseptic was strong the number of colonies could be counted readily. When it was weak, and in the case of the controls, the agar became opaque with innumerable minute colonies. The results were comparative, and did not lend themselves to strict quantitative expression. This was to be expected, for the specimens differed considerably. All were heavily but not equally infected. Some were thick and mucoid, and would not mix well with the antiseptics. However, in the case of every sample of pus, several antiseptics and a control were tested.

I give a few tables to illustrate the kind of result obtained. Using this method, I came to the following conclusions: For the purpose of washing out a wound, neutral hypochlorous solutions are by far the most potent of the antiseptics usually employed, and are effective if diluted to 1 in 800 available chlorine, or 1 in 4 of the strengths usually dispensed. Mercury antiseptics 1 in 1,000, and carbolic acid 1 in 80, never sterilize completely, but kill a very large number of microbes, and delay the appearance of the growth of those which remain. Hydrogen peroxide by itself has very little bactericidal power, but when added to other antiseptics with which it is not incompatible, it increases their bactericidal power on pus organisms, presumably by its mechanical effect. Most of the other organisms in pus are killed more surely than streptococci and staphylococci, an action which is distinctly more marked in the case of mercury and carbolic acid than in the case of iodine and hypochlorous solutions.

TABLE I.—*Showing the Effects of Antiseptics upon the Growth of Bacteria in Pus.*

Experiment I.

Iodine:	1 : 400	1 : 800	1 : 1600	1 : 3200	1 : 6400
16 hours	+	++	+++	+++	++++ gas
Biniodide of mercury:					
16 hours	+	++	++	+++	
40 hours	++	+++	+++	+++	
Carbolic acid:	1 : 40	1 : 80	1 : 160	1 : 320	
16 hours	+	++	+++		
40 hours	++	+++	+++		
Antiseptic diluted with hydrogen peroxide (5 vol.).					
Biniodide of mercury:	1 : 400	1 : 800	1 : 1600	1 : 3200	1 : 6400
20 hours	−	−	+	+++	+++
40 hours	−	−	++	+++	+++
Carbolic acid:	1 : 40	1 : 80	1 : 160	1 : 320	
20 hours	−	+	++	+++	
40 hours	−	++	+++	++++	

Experiment II.

Hypochlorous solutions	1 : 1	1 : 2	1 : 4	1 : 8
Available chlorine ...	1 : 200	1 : 400	1 : 800	1 : 1600
Dakin's solution:				
18 hours	−	−	−	+
3 days	−	−	−	+
Eusol:				
18 hours	−	−	−	+
3 days	−	−	−	++
Carbolic acid:	1 : 80	1 : 160	Control	
	++	+++	++++	

In the case of the film of pus which the mechanical disturbance of washing does not remove, we again have a large quantity of antiseptic acting for a comparatively short time. I considered here that the effect of the antiseptic could be judged by the following experiment: 20 c.mm. of pus were smeared on the surface of agar slopes and allowed to dry. The tubes were then filled with antiseptic lotion so that the films were completely covered. After an interval the antiseptic was poured away and the tubes incubated upside down, so that any excess drained away. The following table (II) illustrates the results:

TABLE II.—*Showing the Effects of Antiseptics upon the Growth of Bacteria in dried Pus.*

Experiment I.

Antiseptic.	Strength.	Time.	
Carbolic acid ...	1 : 80	9 min.	Growth as in control.
Eusol (1 : 200 available chlorine)	1 : 4	1½ min.	All but a few small areas sterilized.
" " ...	1 : 4	3 min.	All but a few small areas sterilized.
" " ...	1 : 4	5 min.	All but a few small areas sterilized.
" " ...	1 : 4	10 min.	All but one small area sterilized.
" " ...	1 : 8	2 min.	Two small sterile areas.
" " ...	1 : 8	5 min.	A few sterile areas.

Experiment II.

Carbolic acid ...	1 : 80	11 min.	Many discrete colonies all over film.
" " ...	1 : 80	40 min.	Sterile.
Iodine	1 : 1000	4 min.	Sterile.
Biniodide of mercury	1 : 1000	4 min.	Sterile.
Hydrogen peroxide	2.5 vol.	10 min.	Sterile.
Dakin's solution (1 : 200 available chlorine)	Undil.	1½ min.	All but a small area sterilized.
" " ...	"	10 min.	Sterile.
" " ...	1 : 2	5 min.	Two colonies.
" " ...	1 : 2	10 min.	Two colonies.
" " ...	1 : 4	5 min.	All but a few small areas sterile.
" " ...	1 : 4	10 min.	All but one small area sterile.
" " ...	1 : 8	10 min.	Good growth; part of film sterile.
Control			Massive growth.

The results are very similar to those of the first experiment. One point was clearly shown, that the thickness of film makes much difference to the efficacy of the antiseptic. It was clear also that some antiseptics were much more rapid in their action than others, notably the hypochlorous solutions. This suggests that these are the most suitable for the purpose of washing out a wound, especially as they have practically no effect on the activity of the leucocytes.

In the case of the dressings, the antiseptic is gradually diluted with pus, becoming at the same time less efficient. Here, therefore, the pus tends to be in excess. To test the effect of antiseptics in these circumstances, I took either a specimen of pus containing very few organisms, one or two per field of a film, or a very thick suspension of blood corpuscles in serum containing a few organisms, and added a proportion of antiseptic. A film was prepared from the mixture, which was then incubated. After a time another film was prepared and compared with the first. If no difference in the number of organisms before and after could be detected, I concluded that the growth was prevented by the antiseptic. If there was a difference, it is clear that the organisms grew in spite of the presence of the antiseptic. A mixture of pus and saline served as control. In the table (III) which I have set out, the strength of the antiseptics given is the ultimate strength in the mixtures. Thus a strength of biniodide of mercury 1 in 1,000 would be present in a mixture of four parts of pus and one part of 1 in 200 of the antiseptic. In these experiments I found it made very much difference whether phagocytosis had taken place or not, there being an advantage in favour of the antiseptic when

TABLE III.—*Showing the Effects of Antiseptics upon the Growth of Bacteria when the Antiseptic is diluted with Pus.*

Experiment I (4 parts of pus, 1 part of antiseptic).		
Carbolic acid	1 : 240− ...	1 : 480+
Hydrogen peroxide (10 vol.)	...	1 : 5+
Iodine	1 : 1000− ...	1 : 2000+
Biniodide of mercury	...	1 : 1000+
Experiment II.		
Iodine:		
3 parts antiseptic, 1 part pus	... 1 : 1600− ...	1 : 3200+
1 part ,, 1 ,, ,,	... 1 : 1600−	
1 ,, ,, 3 parts pus	... ...	1 : 1600+
1 ,, ,, 4 ,, ,,	... ...	1 : 1000+
Biniodide of mercury:		
3 parts antiseptic, 1 part pus	... 1·800− ...	1 : 1600+
1 part ,, 1 ,, ,,	... 1 : 900− ...	1 : 1400+
1 ,, ,, 3 parts pus	... 1 : 800− ...	1 : 1600+
1 ,, ,, 4 ,, ,,	... ...	1 : 1000+
Experiment III (4 parts blood corpuscles with staphylococcus-infected leucocytes, 1 part antiseptic).		
Carbolic acid	1 : 200*− ...	1 : 300+
Chloramine	1 : 75*− ...	1 : 100+
Experiment IV (1 part blood corpuscles, 1 part antiseptic).		
Hypochlorous solutions (1 : 200 available chlorine):		
Dakin's solution ... 1 : 2† (?)	... 1 : 4+ ...	1 : 8+
Eusol ... ... 1 : 2−	... 1 : 4− ...	1 : 8+
Carbolic acid ... ... 1 : 160*−	... 1 : 320+	

* Subcultures on agar gave no growth.
† Subcultures on agar gave a little growth.

it had not—that is, organisms grew better (1) in pus from an infected wound than in sterile pus to which a suspension of microbes was added; (2) in the infected blood when it had been incubated so as to allow phagocytosis to take place. This would lead us to expect that antiseptic dressings would be especially useful (1) in the earlier stages of an infection, before there is much pus; (2) to prevent the growth of organisms which might obtain access to a wound during the dressing. The following are the conclusions which I consider these experments justify: (1) The ultimate strength of the antiseptic being the same, the greater the proportion of pus the less the inhibition of growth. (2) Where pus is present in the proportion of 4 parts to 1 of antiseptic, organisms may grow freely when the following are the antiseptics used: Mercuric salts 1 in 200, carbolic acid 1 in 60, iodine 1 in 200, boracic acid 1 in 20, chloramine 1 in 20, hypochlorous solution 1 in 200 available chlorine. Organisms also grew when salt solution 20 per cent. was used. (3) Since organisms grow in pus in which antiseptics are present in the strengths indicated above, it is utterly unreasonable to expect any of them to diffuse into the tissues to such an extent as will give a strength sufficient to inhibit the growth of microbes, still less to kill them. (4) The pyogenic organisms are, as regard their growth in pus, among the least affected by the ordinary antiseptics.

The results obtained with hypochlorous solutions are of particular interest at present, inasmuch as eusol is being advocated for intravenous injection in cases of septicaemia. If they have any beneficial effect in the blood, it is clear the explanation cannot be found in direct bactericidal action.

When these experiments are reviewed as a whole, it becomes plain that in appraising the value of an antiseptic the purpose for which it is used must be taken into account. For instance, for washing out a wound, when the antiseptic would be in great excess, hypochlorous solutions are very potent, and carbolic acid comparatively weak. On the other hand, for an application in a dressing, when the pus would tend to be in excess, hypochlorous solutions are practically useless, whilst carbolic acid, although it has the disadvantage of interfering with the activity of the leucocytes, is fairly efficient.

Again, it becomes clear that, upon the evidence the experiments supply, antiseptics cannot do as much as is claimed for them. They certainly cannot sterilize the tissues subjacent to the surface of a wound, and, indeed, cannot be depended upon to sterilize an accessible surface, although they kill many of the organisms on it. Their use, therefore, depends on whether there is any advantage in this. It would seem that there is, for it can hardly be possible that the depth and intensity of the tissue infection are independent of the proportion and virulence of the organisms in the surface pus. If, therefore, these can be reduced, even temporarily, without at the same time unduly interfering with physiological processes, it is an important gain. This, which is in fact the most important object in dressing wounds, can be done by means of antiseptics, and herein lies their rôle in antiseptic treatment. If we expect more from the antiseptics at present available, we shall be disappointed.

In conclusion, I would express my grateful acknowledgements to those with whom I have been associated under the auspices of the Army Medical Service, and of the Medical Research Committee; but in particular to my former chief, Colonel Sir Almroth Wright, although I have come to conclusions divergent from many of those at which he has arrived.

REFERENCES.
[1] BRITISH MEDICAL JOURNAL, January 1st, 1916. [2] *British Journal of Surgery*, January, 1916.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

SEVERE CEREBRAL INJURY, ASSOCIATED WITH LAUGHTER.

ON two occasions last summer I saw what I considered an unusual feature connected with the condition of two patients who were brought into an advanced dressing station suffering from severe head injuries. The injuries were in the lower occipital region of the skull, and were caused in one instance by shrapnel, in the other by high explosive. The shrapnel had caused a small fracture of the occipital bone, through which blood oozed, and the high explosive some bruising of the back of the head and neck. The men suffered from very severe shock and were quite unconscious of their surroundings, but exhibited the rather striking combination of a rambling and muttering delirium, associated with mild and frequent laughter.

There was here the suggestion of a continuous stimulation of the emotional centre for laughter, and as laughter is a modified form of respiration, an injury to some area near the respiratory centre in the floor of the fourth ventricle might account for the condition. The difficulty is that high explosive tends to spread its energies, and other centres of the brain may have suffered from concussion.

According to Sherrington (Schäfer's *Textbook of Physiology*) the respiratory apparatus is in the higher groups subservient to the emotional and mental expression, and he states that the bulb possesses inhibition to a great extent.

Nitrous oxide over-stimulates the respiratory centre and causes laughter, but, as in the case of chloroform and alcohol, the accepted opinion is that the preliminary excitement is due, not to stimulation of the brain areas, but to lessened activity of the functions of control and restraint. But a direct stimulation of the emotional centres is possible, and injury may reveal the truth where experimental work is impossible.

Edinburgh. J. M. MACPHAIL, M.D.Edin.

EARLY DIAGNOSIS OF WHOOPING-COUGH.

WITH reference to the memorandum from Dr. H. W. Jacob (April 22nd, p. 589), I would recommend him to have a blood count made in all suspected cases of whooping-cough. In all true cases of whooping-cough there will be found a marked lymphocytosis, and this is present some considerable time before the development of the characteristic cough. It is also helpful in the diagnosis of those cases in which the characteristic cough is absent or not heard. I am unfortunately not able to give any references to the literature on the subject.

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British Expeditionary Force.

THE *Boston Medical and Surgical Journal* states that when the United States undertook the treatment of leprosy in the Philippines there were about 600 cases in the islands. The island of Culion, which afforded excellent opportunities for agricultural work, was chosen as a place of segregation. Four hundred dwelling-houses, a theatre, a town hall, a school, and a harbour were built, and provided with a water supply and with sewerage and lighting systems. The colony now numbers about 3,500 lepers. They are given all possible liberty, organize their own police force, elect their own mayor and council, and take some care of the island. Attempts to interest them in cultivation of the land were indifferently successful, and a plan to induce them to take up cattle breeding—cattle being insusceptible of leprosy—is now under consideration. Treatment by chaulmoogra oil has given encouraging results; and already twenty-three lepers have been discharged as cured.